

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of : *Velikyan et al.*

Application No. : 10/552,206

Filing Date : September 14, 2006

Art Unit : 1618

Title : Method of Obtaining Gallium-68 and Use Thereof and Device for
Carrying Out Said Method

Docket No. : PZ0333

Mail Stop Appeal Brief–Patents

Commissioner for Patents

P.O. Box 1450

Alexandria VA 22313-1450

APPEAL BRIEF

Appeal Brief
Serial No.: 10/552,206
Attorney Docket No.: PZ0333

I. REAL PARTY IN INTEREST

The real party in interest in this Appeal is GE Healthcare, Inc., a part of General Electric ("GE").

II. RELATED APPEALS AND INTERFERENCES

There are no other appeals or interferences related to the instant appeal.

III. STATUS OF CLAIMS

Claims 1-19 are pending in this application. The Examiner has rejected all of these claims. Claims 1-19 as amended during prosecution are reproduced in the **Claims Appendix** attached hereto. Appellants are appealing the rejection of Claims 1-19.

IV. STATUS OF AMENDMENTS

A final Office Action was mailed on March 23, 2010. No claims have been amended thereafter.

V. SUMMARY OF CLAIMED SUBJECT MATTER

Independent Claim 1 describes a method of obtaining ^{68}Ga by (i) elution of a $^{68}\text{Ge}/^{68}\text{Ga}$ generator to provide a supply of eluate containing ^{68}Ga ; (ii) contacting said eluate with an anion exchanger comprising HCO_3^- as counterions, so that the ^{68}Ga from step (i) binds to said anion exchanger; and (iii) eluting the bound ^{68}Ga of step (ii) from said anion exchanger. Support for this claim can be found on page 3, lines 24 to page 4 line 26. of the specification.

Independent claim 15 describes a kit for the preparation of ^{68}Ga from a $^{68}\text{Ge}/^{68}\text{Ga}$ generator, which comprises a generator column and a second column that comprises an anion exchanger comprising HCO_3^- as counterions.

Support for this claim can be found on page 8, line 14 to line 16 of the specification.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The issues for review in this appeal arise from an Office Action dated March 23 2010. The Examiner rejected claims 1-19 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Griffiths et al., WO03/059397A2 (“Griffiths”) in view of Bottcher et al., US 5,439,863 (“Bottcher”) and further in view of Maier-Borst et al., GB2056471A (“Maier-Borst”) and Wheaton et al., Industrial and Engineering Chemistry, 1951, 43, 1088-93 (“Wheaton”).

The Examiner also rejected claims 1, 3-7, and 15-17 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Maier-Borst et al., GB2056471A (“Maier-Borst”) in view of Therefore, the issues in this appeal are:

1. Whether Griffiths in view of Bottcher and in further view of Maier-Borst and Wheaton disclose, teach, or suggest all the elements of claims 1-19? And
2. Whether Maier-Borst in view of Wheaton disclose, teach, or suggest the elements of claims 1, 3-7, and 15-17?

VII. ARGUMENT

The Examiner rejected Claims 1-19 under 35 U.S.C. § 103 (a) as allegedly being unpatentable over Griffiths et al., WO03/059397A2 (“Griffiths”) in view of Bottcher et al., US 5,439,863 (“Bottcher”) and further in view of Maier-Borst et al., GB2056471A (“Maier-Borst”) and Wheaton et al., Industrial and Engineering Chemistry, 1951, 43, 1088-93 (“Wheaton”).

The Examiner also rejected claims 1, 3-7, and 15-17 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Maier-Borst et al., GB2056471A (“Maier-Borst”) in view of Wheaton et al., Industrial and Engineering Chemistry, 1951, 43, 1088-93 (“Wheaton”).

Appellants respectfully request that The Board of Patent Appeals and Interferences (“Board”) should reverse the Examiner’s rejection for the reasons set forth below.

A. The Examiner’s Rejection of Claims 1-19 Should be Reversed Since Griffiths in view of Bottcher and in further view of Maier-Borst and Wheaton Fails to Disclose, Teach or Suggest All the Elements of Claims 1-19.

The Examiner’s Rejections of Claims 1-19 should be reversed since Griffiths in view of Bottcher and in further view of Maier-Borst and Wheaton fail to disclose, teach, or suggest all the elements of claims 1-19.

In the Office Action dated March 23, 2010, the Examiner states that the following are obvious:

- (i) to use the microwave activation method of Bottcher in the ⁶⁸Ga-DOTA-peptide complex formation of Griffiths;

- (ii) to use the anion exchanger taught by Maier-Borst to separate ^{68}Ga from ^{68}Ge when eluting a radioisotope generator having an aluminum oxide column – to avoid eluting with EDTA and having to destroy a ^{68}Ga -EDTA complex; and
- (iii) that the separation of ^{68}Ga from ^{68}Ge using an anion exchange resin comprising quaternary ammonium groups may comprise bicarbonate as the counterion, since Wheaton teaches that “...provides for a minimal amount of swelling and thus greater selectivity”.

Objection (i)

First, the objection based on Bottcher is apparently directed at present claim 13 (only), since that is the only claim wherein ^{68}Ga -metal complex formation using microwave activation are essential features.

Although Griffiths teaches ^{68}Ga metal complex formation, Griffiths is silent on anion exchangers using HCO_3^- or containing amine functional groups or based on polystyrene-divinylbenzene. Hence, the combination [Maier-Worst + Wheaton + Griffiths] does not provide all the essential features of present claims 8 to 12, 14, 18 and 19. Similar logic applies to claim 13, since the combination [Maier-Worst + Wheaton + Griffiths + Bottcher] does not provide all the essential features of present claim 13.

Put another way, Griffiths and Bottcher individually or together, cannot remedy the deficiencies of Maier-Worst and Wheaton with respect to present claims 1-19.

Consequently, the obviousness rejection should be withdrawn.

Objection (ii)

The combination [Maier-Worst + Wheaton + prior art cited by Maier-Worst] does not provide all the essential features of present claim 2.

Secondly, the Examiner refs to page 1 lines 10-18 of Maier-Worst. The prior art ^{68}Ga generator

referred to there uses an aluminum oxide column (line 12). Present claim 2 has a titanium dioxide column as an essential feature. That is completely different to aluminum oxide. Hence, for that reason also the combination does not provide all the essential features of present claim 2.

Additionally, the Examiner has argued that the obvious combination [Maier-Worst + Wheaton + prior art cited by Maier-Worst] provides $^{68}\text{Ga}/^{68}\text{Ge}$ separation using an aluminum oxide column. That teaches away from the subject matter of present claim 2, and is thus positive evidence in favor of an inventive step for claim 2.

Consequently, obviousness rejection (ii) should also be withdrawn.

Objection (iii).

This objection apparently reiterates the objection of Maier-Worst + Wheaton (please see below part B), and has been dealt with there.

Obviousness rejection (iii) should therefore also be withdrawn.

Additionally, Appellants wish to point out that “the prior art itself must provide a motivation or reason for the worker in the art, without the benefit of the Applicant’s specification, to make necessary changes in the reference device”. See, *Ex parte Chicago Rawhide Manufacturing Co.*, 226 U.S.P.Q. 438 (PTO Bd. App. 1984). Additionally, it is impermissible within the framework of 35 U.S.C. §103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art. *Bausch & Lomb, Inc. v. Barnes-*

Hind/Hydrocurve, Inc., 796 F.2d 443 (Fed. Cir. 1986). (emphasis added).

It is therefore respectfully submitted that the 35 U.S.C. 103(a) rejections of claims 1-19 as being unpatentable over Griffiths in view of Bottcher in further view of Maier-Borst and Wheaton be withdrawn.

B. The Examiner's Rejection of Claims 1, 3-7 and 15-17 Should be Reversed Since Maier-Borst in view of Wheaton Fails to Disclose, Teach or Suggest All the Elements of Claims 1-19.

Claims 1, 3-7 and 15-17 stand rejected as obvious over Maier-Borst *et al* (GB 2056471 A) in view of Wheaton [Indust.Eng.Chem., 43, 1088-1093 (1951)].

One skilled in the art would not be motivated to choose bicarbonate from the resin counterions taught by Wheaton in the anion exchanger comprising quaternary ammonium groups of Maier-Borst *et al*, since Wheaton teaches that bicarbonate provides for a "...minimal amount of swelling and thus greater selectivity...". If one skilled in the art were assumed to choose the counterion for the ionic form of the anion exchange resin based on minimizing the swelling characteristics, then Table I (page 1089) of Wheaton teaches that the following 5 resins would all have superior characteristics to bicarbonate:

- (i) iodide;
- (ii) bromide;
- (iii) nitrate;
- (iv) nitrite; and

(v) chloride.

Hence, Appellants contend that the person skilled in the art, if *arguendo* assumed to be seeking to modify Maier-Borst based on resin selectivity as taught by Wheaton, would choose one or more of iodide, bromide, nitrate, nitrite or chloride ahead of bicarbonate. The facts are that Wheaton clearly teaches that 5 other resin counterions would be expected to have superior characteristics to bicarbonate. The motivation for the person skilled in the art stems from an expectation of improved results. It would not be practical to combine Maier-Borst and Wheaton and yet ignore the clear teaching of Wheaton on 5 resins with reported superior selectivity. The practical combination of Maier-Borst and Wheaton would therefore clearly teach away from the presently claimed subject matter.

Present claim 1 is therefore believed to be nonobvious over the combination of Maier-Borst and Wheaton. By definition, dependent claims 2 to 7 are also believed non-obvious. Claims 8 and 15 are independent claims, which both refer to claim 1 and hence contain all the essential features of claim 1. They, and their associated dependent claims (9-14 and 16-17 respectively) are therefore believed nonobvious for the same reasons.

The obviousness rejection of present claims 1, 3-7 and 15-17 based on combination of Maier-Borst and Wheaton should therefore be withdrawn.

DOUBLE PATENTING

Claims 1, 2, and 6-14 are provisionally rejected as claiming the same invention as that of claims 1-15 of co-pending Application No. 10/552,134. In response, Applicants submit that claims will be amended or cancelled if the instant application is indicated to be allowable.

Further, claims 1, 2, and 6-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, and 7-13 of copending Application No. 11/358,681. In response, Applicants submit that a terminal disclaimer will be filed once the instant application is indicated to allowable.

CONCLUSION

In view of the foregoing, Appellants respectfully request that the Board reverse the rejections of Claims 1-19 as set forth in the Office Action mailed March 23,, 2010, that the Board allow the pending claims since they are in condition for allowance, and that the Board grant any other relief as it deems proper.

Dated: August 23, 2010

Respectfully submitted,

/Craig M. Bohlken/
Craig M. Bohlken
Reg.No.52,628
GE Healthcare, Inc.
101CarnegieCenter
Princeton,NJ08540-6231
Phone No.: (609) 514-6530

VIII. CLAIMS APPENDIX

1. A method of obtaining ^{68}Ga by:
 - (i) elution of a $^{68}\text{Ge}/^{68}\text{Ga}$ generator to provide a supply of eluate containing ^{68}Ga ;
 - (ii) contacting said eluate with an anion exchanger comprising HCO_3^- as counterions, so that the ^{68}Ga from step (i) binds to said anion exchanger; and
 - (iii) eluting the bound ^{68}Ga of step (ii) from said anion exchanger.
2. The method according to claim 1 wherein the $^{68}\text{Ge}/^{68}\text{Ga}$ generator of step (i) comprises a column comprising titanium dioxide.
3. The method according to claim 1 wherein in step (i), 0.05 to 5 M HCl is used to elute ^{68}Ga from the $^{68}\text{Ge}/^{68}\text{Ga}$ generator.
4. The method according to claim 2 wherein in step (i), 0.05 to 0.1 M HCl is used to elute ^{68}Ga from the $^{68}\text{Ge}/^{68}\text{Ga}$ generator.
5. The method according to claim 1 wherein in step (iii), water is used to elute ^{68}Ga from the anion exchanger.
6. The method according to claim 1 wherein the anion exchanger is an anion exchanger comprising quaternary amine functional groups.
7. The method according to claim 1 wherein the anion exchanger is an anion exchange resin based on polystyrene-divinylbenzene.
8. Method of producing a ^{68}Ga -radiolabelled complex by reacting ^{68}Ga obtained by the method according to claim 1 with a chelating agent.
9. Method according to claim 8 wherein the chelating agent is a macrocyclic chelating agent.

10. Method according to claim 8 wherein the chelating agent comprises hard donor atoms, preferably O and N.
11. Method according to claim 8 wherein the chelating agent is a bifunctional chelating agent
12. Method according to claim 11 wherein the chelating agent is a bifunctional chelating agent comprising a targeting vector selected from the group consisting of proteins, glycoproteins, lipoproteins, polypeptides, glycopolypeptides, lipopolypeptides, peptides, glycopeptides, lipopeptides, carbohydrates, nucleic acids, oligonucleotides or a part, a fragment, a derivative or a complex of the aforesaid compounds and small organic molecules.
13. Method according to claim 8 wherein the reaction is carried out using microwave activation.
14. Method according to claim 8 for the production of ^{68}Ga -radiolabelled PET tracers.
15. Kit for the preparation of ^{68}Ga from a $^{68}\text{Ge}/^{68}\text{Ga}$ generator, which comprises a generator column and a second column that comprises an anion exchanger comprising HCO_3^- as counterions.
16. Kit according to claim 15 further comprising means to couple the columns in series.
17. Kit according to claim 15 further comprising aqueous HCl to elute the ^{68}Ga from the generator column and/or water to elute the ^{68}Ga from the anion exchanger column, preferably, the HCl and the water being aseptically and in a hermetically sealed container.
18. Kit according to claim 15 further comprising a chelating agent, preferably a bifunctional chelating agent.
19. A method of using a kit according to claim 18 for the production of ^{68}Ga -radiolabelled PET tracers, comprising producing a ^{68}Ga -radiolabelled complex by reacting ^{68}Ga obtained by the method according to claim 1 with the chelating agent.

IX. EVIDENCE APPENDIX

Appellants hereby present the following publications/patents:

WO03/059397A2 (Griffiths et al.);

US 5,439,863 (Bottcher);

GB2056471A (Maier-Bost); and

Indust.Eng.Chem., 43, 1088-1093, 1951 (Wheaton).

This is the evidence relied upon by the Examiner for rejection of appealed Claims 1-19 in the final Office Action dated March 23, 2010.

X. RELATED PROCEEDINGS APPENDIX

There are no other appeals or interferences related to the instant appeal